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Impact of the national targeted Hepatitis A immunisation program in Australia: 2000–2014

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ABSTRACT

In November 2005, hepatitis A vaccine was funded under the Australian National Immunisation Program for Aboriginal and Torres Strait Islander (Indigenous) children aged 12–24 months in the targeted jurisdictions of Queensland, South Australia, Western Australia and the Northern Territory.

We reviewed the epidemiology of hepatitis A from 2000 to 2014 using data from the Australian National Notifiable Diseases Surveillance System, the National Hospital Morbidity Database, and Australian Bureau of Statistics causes-of-death data. The impact of the national hepatitis A immunisation program was assessed by comparison of pre-vaccine (2000–2005) and post-vaccine time periods (2006–2014), by age group, Indigenous status and jurisdiction using incidence rate ratios (IRR) per 100,000 population and 95% confidence intervals (CI).

The national pre-vaccine notification rate in Indigenous people was four times higher than the non-Indigenous rate, and declined from 8.41 per 100,000 (95% CI 5.03–11.79) pre-vaccine to 0.85 per 100,000 (95% CI 0.00–1.99) post-vaccine, becoming similar to the non-Indigenous rate. Notification and hospitalisation rates in Indigenous children aged <5 years from targeted jurisdictions declined in the post-vaccine period when compared to the pre-vaccine period (notifications: IRR = 0.07; 95% CI 0.04–0.13; hospitalisations: IRR = 0.04; 95% CI 0.01–0.16). As did notification rates in Indigenous people aged 5–19 (IRR = 0.08; 95% CI 0.05–0.13) and 20–49 years (IRR = 0.06; 95% CI 0.02–0.15) in targeted jurisdictions. For non-Indigenous people from targeted jurisdictions, notification rates decreased significantly in children aged <5 years (IRR 0.47; 95% CI 0.31–0.71), and significantly more overall (IRR = 0.43; 95% CI 0.39–0.47) compared to non-Indigenous people from non-targeted jurisdictions (IRR = 0.60; 95% CI 0.56–0.64).

The national hepatitis A immunisation program has had a significant impact in the targeted population with relatively modest vaccine coverage, with evidence suggestive of substantial herd protection effects.

1. Introduction

Hepatitis A causes significant morbidity globally (affecting approximately 120 million people annually [1]), with the incidence of disease usually inversely correlated with level of sanitation and access to safe drinking water [2–4]. With improving sanitation and living conditions in Australia, the annual notification rate of hepatitis A has declined from 123 notifications per 100,000 population in 1961 to 1 per 100,000 population in 2014 [5,6]. A number of person-to-person and foodborne outbreaks of hepatitis A have occurred in Australia over the past twenty years, including very large outbreaks associated with raw oysters (1997) and semi-dried tomatoes (2009) [7–15].

Hepatitis A vaccine was first registered for use in Australia in 1994 and has since been recommended for high-risk groups [16]. In response to an increasing number of hepatitis A cases and the death of three Aboriginal and Torres Strait Islander (henceforth referred to as Indigenous) children in north Queensland, a hepatitis A immunisation program commenced in February 1999 for all Indigenous children in this region (north Queensland has a population of approximately 600,000 people, of which 1.2% are Indigenous children aged under 5 years) [17,18]. Two doses of hepatitis A vaccine were scheduled at 18 and 24 months of age,

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and catch-up vaccination recommended for children <6 years of age [16,17]. Following the north Queensland program, a rapid decline in hepatitis A notifications was reported in the Indigenous and non-Indigenous populations [17].

In November 2005, hepatitis A vaccine was funded under the Australian National Immunisation Program (NIP) for all Indigenous children aged 12–24 months residing in four of the eight states and territories of Australia, namely Queensland, South Australia, Western Australia and the Northern Territory, due to a high risk of acquiring hepatitis A and hospitalisation from it [16]. Two doses were originally scheduled at 12 months and 18 months of age in the Northern Territory and Western Australia, and at 18 and 24 months of age in Queensland and South Australia, changing to 12 and 18 months of age in all four jurisdictions in July 2013 [16,19]. Over the period 2006–2010, decreases in hepatitis A notifications in the Indigenous Australian population was reported [20]. These decreases in targeted jurisdictions occurred in the context of relatively modest hepatitis A vaccination coverage in Indigenous children before 36 months of age, with two-dose coverage increasing from 31% in 2007 to 60% in 2013, and one-dose coverage at 71% during 2013 [19,20].

The aim of our study was to review the epidemiology of hepatitis A in Australia from 2000 to 2014, focusing on the impact of the national hepatitis A immunisation program on both the directly targeted population (Indigenous children in the targeted jurisdictions) and broader herd protection effects Australia-wide.

2. Methods

2.1. Study design and study period

We undertook a descriptive epidemiological study, with comparison of notifications and hospitalisations in the period before (2000–2005) and after (2006–2014) the introduction of the targeted hepatitis A immunisation program in Australia.

2.2. Data sources

2.2.1. Notifications

Confirmed and probable cases of hepatitis A are notifiable to the National Notifiable Diseases Surveillance System (NNDSS) under the public health legislation of each jurisdiction [21]. A confirmed case of hepatitis A requires either laboratory definitive evidence (detection of hepatitis A virus by nucleic acid testing); or laboratory suggestive evidence (detection of hepatitis A-specific immunoglobulin M antibodies in the absence of recent vaccination) plus clinical evidence; or laboratory suggestive evidence plus epidemiological evidence (contact between two people involving a plausible mode of transmission at a time when one of them is likely to be infectious and the other has an illness that started within 15–50 days after this contact and at least one case in the chain of epidemiologically linked cases is laboratory confirmed) [22]. A probable case requires clinical evidence plus epidemiological evidence [22].

For this analysis, notification data included all confirmed and probable cases of hepatitis A from the NNDSS with an onset date between 1 January 2000 and 31 December 2014. For cases with no recorded onset date, we used the earliest recorded date among the fields of date of specimen, date of notification, and date when the notification was received. Variables extracted comprised onset date, age, sex, jurisdiction of residence, Indigenous status, place of acquisition, whether died from disease, and vaccination status. The analysis of the 'place of acquisition' data field was restricted to the years 2010–2014, where data completeness was 80% or greater.

2.2.2. Hospitalisations

The National Hospital Morbidity Database (NHMD) is an administrative database maintained by the Australian Institute of Health and Welfare. Private and public hospital discharge summaries are used to capture data relating to administrative, demographic and clinical information on patients hospitalised in Australia [21]. Using the International Statistical Classification of Disease and Related Health Problems, 10th Revision, Australian Modification (ICD-10-AM) code B15 (hepatitis A), all eligible hospital admissions coded as hepatitis A (either as the principal or other diagnosis) and with an admission date between 1 January 2000 and 31 December 2013 (latest data available) were included in this analysis.

Variables extracted comprised primary or other diagnosis, date of admission, age, sex, jurisdiction of residence, Indigenous status, length of stay (bed days) and mode of separation from hospital. Jurisdiction of residence and age specific hospitalisation data were only available between 1 January 2000 and 30 June 2012.

2.2.3. Mortality

Mortality data related to hepatitis A were obtained from the NNDSS, NHMD and the Australian Bureau of Statistics (ABS). ABS causes of death data included in this analysis were deaths due to hepatitis A (ICD-10: code B15) as the primary underlying cause, for deaths registered between 2007 and 2011 (latest data available).

2.2.4. Population estimates

National, jurisdictional, age-specific and Indigenous-specific mid-year estimates of resident population sizes were obtained from the ABS [23].

2.3. Data analysis

We compared notification and hospitalisation rates for two time periods, i.e. before the introduction of the hepatitis A targeted immunisation program (pre-vaccine 2000–2005) and after (post-vaccine 2006-latest available data), and for targeted (Queensland, South Australia, Western Australia and the Northern Territory) and non-targeted (New South Wales, Victoria, Tasmania and the Australian Capital Territory) jurisdictions.

Notification and hospitalisation rates were calculated using ABS population estimates as the denominator and are presented as age-specific, jurisdiction-specific, or Indigenous-specific subpopulation rates per 100,000 population. Descriptive statistics included median age (and range) and average length of hospital stay. Place of acquisition for Indigenous and non-Indigenous people was compared and tested for significance using a Fisher's exact test. Age-specific incidence rate ratios (IRR), 95% confidence intervals (95% CI) and p-values were calculated for Indigenous and non-Indigenous populations at the national level, and for targeted and non-targeted jurisdictions, assuming a Poisson distribution. If the 95% CI for any age-specific or total IRR did not overlap with the corresponding comparison group, this was considered evidence of a difference beyond that expected from random variation. Analyses were conducted using STATA software (version 13.1; StataCorp, College Station, Texas USA).

Ethical approval was not required as de-identified aggregated population-based data were used for routine public health surveillance purposes only.

3. Results

3.1. Secular trends

A total of 5096 hepatitis A notifications were recorded in the NNDSS between January 2000 and December 2014, of which

5004 (98%) were confirmed and 92 (2%) were probable cases. The overall national notification rate declined from 4.25 per 100,000 in 2000 to 0.97 per 100,000 in 2014, with a nadir of 0.65 per 100,000 in 2011. The national notification rate in Indigenous people declined from 8.41 per 100,000 (95% CI 5.03–11.79) during the pre-vaccine period to 0.85 per 100,000 (95% CI −0.28 to 1.98) during the post-vaccine period, while the notification rate in non-Indigenous people declined from 2.24 per 100,000 (95% CI 1.22–3.25) pre-vaccine to 1.17 per 100,000 (95% CI 0.71–1.63) post-vaccine.

In the NHMD, 3398 hospitalisations were recorded between January 2000 and December 2013 with a diagnosis that included hepatitis A. The overall national hospitalisation rate declined from 2.31 per 100,000 in 2000 to 0.89 per 100,000 in 2013, with a nadir of 0.53 per 100,000 in 2012. The national hospitalisation rate in Indigenous people declined from 4.23 per 100,000 (95% CI 3.52–4.94) during the pre-vaccine period to 1.09 per 100,000 (95% CI 0.46–1.73) during the post-vaccine period, while the hospitalisation rate in non-Indigenous people declined from 1.45 per 100,000 (95% CI 0.95–1.96) pre-vaccine to 0.87 per 100,000 (95% CI 0.62–1.13) post-vaccine. Of the 3398 hospitalisations, 1781 (52%) had hepatitis A identified as the primary diagnosis, with a median length of stay of 3 days for these 1781 hospitalisations (range: 1–55 days).

Eight deaths (age range 5–⩾65 years) were recorded by the ABS between 2007 and 2011 with hepatitis A as the primary underlying cause (data available for post-vaccine period only); six of these deaths were of people aged ⩾65 years. Fewer deaths were recorded in the other data sources; NNDSS (2000–2014) and NHMD (2000–2013) captured five deaths each. Matching of deaths between data sources was not possible using the data fields available.

3.2. Age and sex distribution

The median age of notified and hospitalised hepatitis A cases in Australia was similar between the pre-vaccine (notifications: 28 years, range 0–93; hospitalisations: 41 years, range 0–93) and post –vaccine periods (notifications: 27 years, range 0–97; hospitalisations: 41 years, range 0–97). Overall, 6.9% of notified and 2.7% of hospitalised cases were aged <5 years. The average male to female notification ratio was 1.61:1 (range 1.16:1–2.54:1) in the pre-vaccine period, and 1.21:1 (range 0.95:1–1.47:1) in the post-vaccine period.

3.3. Indigenous status

Between 2000 and 2014, 6% (326/5096) of people notified with hepatitis A were recorded as Indigenous, 77% (3895/5096) as non-Indigenous and 17% (875/5096) as unknown or missing Indigenous status. Completeness of this data field was higher for the targeted jurisdictions (87% complete; 1807/2073) than non-targeted jurisdictions (80% complete; 2418/3023). Of people hospitalised with hepatitis A between 2000 and 2013, 6% (196/3398) were recorded as Indigenous, 92% (3137/3398) as non-Indigenous and 2% (65/3398) as unknown or missing Indigenous status. Between January 2000 and June 2012, completeness of this data field was slightly higher for the non-targeted jurisdictions (99% complete; 1877/1899) than targeted jurisdictions (97% complete; 1118/1158).

3.4. Vaccination status

Of all notifications (N = 5096), 13 (0.3%) were reported as fully vaccinated (three during the pre-vaccine period and ten during the post-vaccine period), 36 (0.7%) as partially vaccinated (four during the pre-vaccine period and 32 during the post-vaccine period), and 5047 (99%) were of unknown vaccination status.

3.5. Place of acquisition

Of the 882 notifications with a recorded place of acquisition between 2010 and 2014, 72% (638/882; annual range 56–87%) were acquired overseas. Common places of overseas acquisition included the Oceania region (15.2% [134/882]), southern-east Asia (17.1% [151/882]) and southern-central Asia (21.3% [188/882]). The proportion of hepatitis A notifications acquired overseas was significantly higher in non-Indigenous people (73%; 636/874) than in Indigenous people (25%; 2/8) ($p > 0.05$).

3.6. Jurisdiction

3.6.1. Targeted jurisdictions (Queensland, Northern Territory, South Australia and Western Australia)

In the targeted jurisdictions, notifications dropped from 411 in 2000 (rate 2.2 per 100,000) to 73 in 2014 (0.3 per 100,000), and hospitalisations from 188 in 2000 (1.0 per 100,000) to 24 during the first half of 2012 (0.1 per 100,000) (Fig. 1). Between 2000 and 2005, Indigenous people residing within targeted jurisdictions had an 11.6 times higher notification rate, and a 3.9 times higher hospitalisation rate of hepatitis A than Indigenous people residing within non-targeted jurisdictions (Table 1).

The notification rate in Indigenous people residing within targeted jurisdictions declined by 93% overall (IRR = 0.07; 95% CI 0.05–0.10) in the post-vaccine period. Age-specific declines were also identified (Table 1). The overall notification rate in non-Indigenous people declined by 57% (IRR = 0.43; 95% CI 0.39–0.47) (Table 1). Hospitalisations in Indigenous people declined by 82% overall (IRR = 0.18; 95% CI 0.12–0.27). Age-specific declines were also identified (Table 1). In non-Indigenous people, the overall hospitalisation rate declined by 46% (IRR = 0.54; 95% CI 0.48–0.62) (Table 1).

The largest decreases in notification and hospitalisation rates were in the Northern Territory (88% and 86%, respectively) and Western Australia (70% and 64%, respectively) (Fig. 2).

3.6.2. Non-targeted jurisdictions (New South Wales, Victoria, Tasmania and the Australian Capital Territory)

Notifications in Indigenous people residing in non-targeted jurisdictions declined by 53% (IRR = 0.47; 95% CI 0.23–0.95) in the post-vaccine period. An age-specific decline of 68% was identified for the 5–19 years age group (IRR = 0.32; 95% CI 0.11–0.95), while there were no notifications in children aged <5 years during the entire study period. Notifications in non-Indigenous people declined by 40% (IRR = 0.60; 95% CI 0.56–0.64). No significant reduction was identified in the non-Indigenous <5 years age group (IRR = 0.96; 95% CI 0.69–1.33) (Table 1).

Hospitalisations in Indigenous people declined by 30% however, this was not statistically significant (IRR = 0.70; 95% CI 0.38–1.27), while hospitalisations in non-Indigenous people declined by 33% (IRR = 0.67; 95% CI 0.61–0.73) (Table 1).

4. Discussion

In the population directly targeted by the national hepatitis A immunisation program in Australia (Indigenous children aged <5 years residing in targeted jurisdictions), we documented significant declines in hepatitis A notification and hospitalisation rates (93% and 96%, respectively) between the pre- and post-vaccine periods. The program also appears to have provided substantial herd protection to both the Indigenous and non-Indigenous popu-

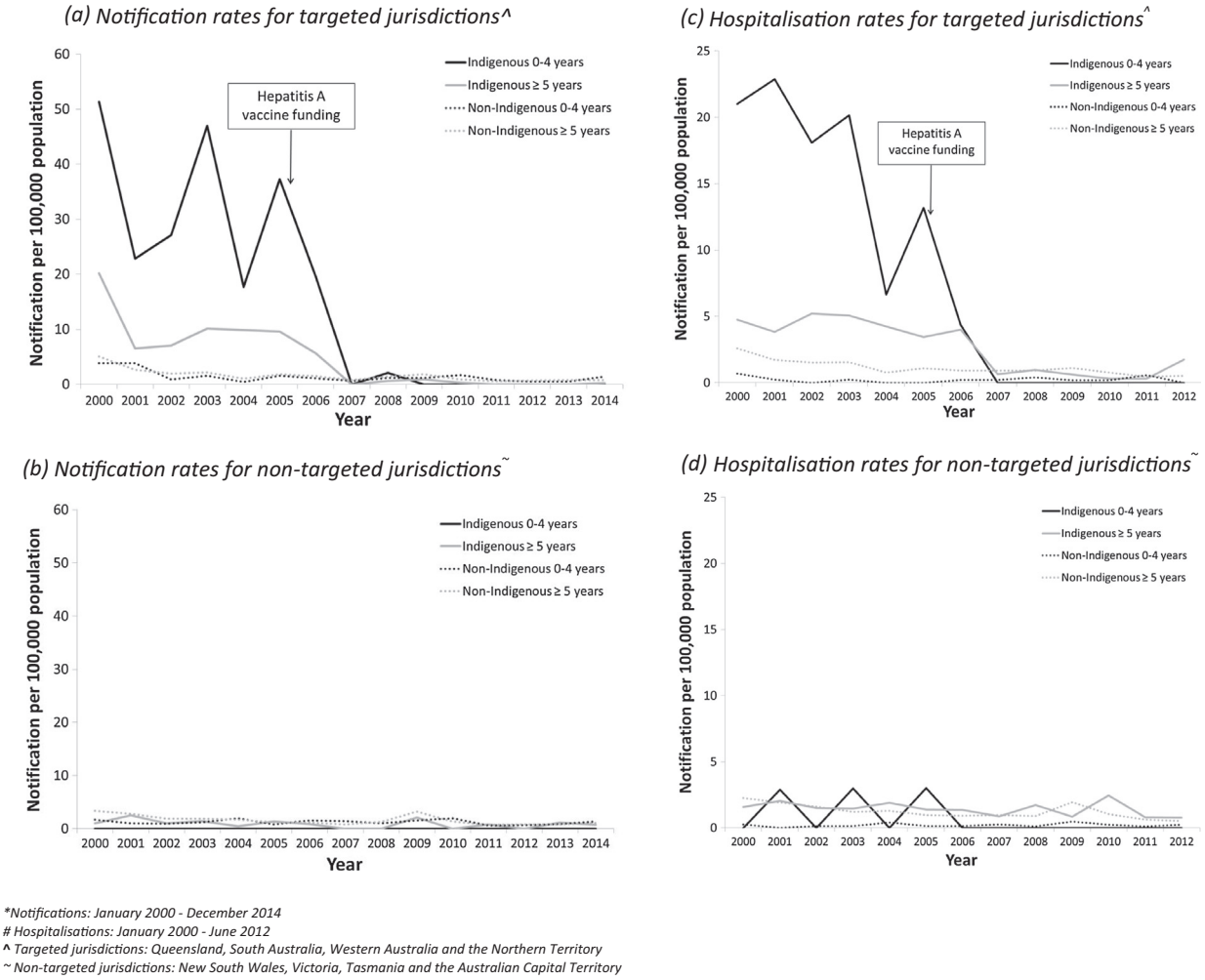

Fig. 1. Targeted and non-targeted hepatitis A notification (*Notifications: January 2000 - December 2014*) and hospitalisation (*Hospitalisations: January 2000 - June 2012*) rates of Australia, by Indigenous status, age group and year. (a) Notification rates for targeted jurisdictions (*Targeted jurisdictions: Queensland, South Australia, Western Australia and the Northern Territory*). (b) Notification rates for non-targeted jurisdictions (*Non-targeted jurisdictions: New South Wales, Victoria, Tasmania and the Australian Capital Territory*). (c) Hospitalisation rates for targeted jurisdictions (*Targeted jurisdictions: Queensland, South Australia, Western Australia and the Northern Territory*). (d) Hospitalisation rates for non-targeted jurisdictions (*Non-targeted jurisdictions: New South Wales, Victoria, Tasmania and the Australian Capital Territory*).

lations aged 5–49 years within targeted jurisdictions. Notification rates declined in the post-vaccine period by 92% for the 5–19 years Indigenous age group, and by 94% for the 20–49 years age group, compared to 68% and 33%, respectively, in non-targeted jurisdictions, with the decrease being significantly different to the non-targeted jurisdictions for the latter age group. In non-Indigenous people, the notification rate in targeted jurisdictions decreased by 51% for children aged <5 years, and by 57% overall, with the overall decrease being significantly different to the overall decrease in non-targeted jurisdictions.

These decreases in targeted jurisdictions occurred in the context of relatively modest hepatitis A vaccination coverage in Indigenous children [24,25]. Young children play a key role in the transmission of hepatitis A to other children and adults, as they are usually asymptomatic (or only mildly symptomatic) and have lower levels of personal hygiene [17,18,26]. We also documented significant, albeit lower, decreases in hepatitis A notifications between the pre- and post-vaccine periods in both Indigenous and non-Indigenous populations in non-targeted jurisdictions (53% and 40%, respectively). These decreases may also be partly attributable to the targeted national immunisation program, given the extensive population movement of Indigenous people between states and territories of Australia [27].

The national targeted hepatitis A immunisation program appears to have been highly effective at reducing the incidence of disease in Australia. However, the descriptive nature of our study makes it difficult to quantify the exact contribution of this program. Of note, the funding of a hepatitis A immunisation program in north Queensland from 1999 (with estimated two-dose coverage of 77% in the Indigenous birth cohort for the year 2000 [17]) may have led us to underestimate the true impact of the national targeted program. Other factors, including the targeted immunisation of high-risk groups (such as travellers to hepatitis A endemic areas, and people with an increased risk of exposure to hepatitis A based on their occupation or lifestyle) as recommended in the Australian Immunisation Handbook [16], may also have contributed to the declines Australia-wide. However, available information indicates that hepatitis A vaccination coverage of adults in high-risk groups such as travellers to hepatitis A endemic areas, although recommended since 1994, is relatively low [28,29]. More general limitations of the data we analysed are that hepatitis A notifications may underestimate true incidence, particularly in young children, and may be influenced by changes in diagnostic and public health follow-up practices over time and across jurisdictions, while hospitalisation data can be influenced by access to hospital care, changes in admission practices, and cod-

Table 1
Hepatitis A notifications and hospitalisations, by age group, Indigenous status and pre-/post-vaccine period, Australia, 2000–2014; rates, counts and incidence rate ratios (95% CI).

	Age group (years)	Pre-vaccine (2000–2005)		Post-vaccine [a]		Incidence rate ratio[b]	
		Non-Indigenous[c] (N)	Indigenous[c] (N)	Non-Indigenous[c] (N)	Indigenous[c] (N)	Non-Indigenous (95% CI)	Indigenous (95% CI)
(a) Targeted jurisdictions: Queensland, South Australia, Western Australia and the Northern Territory							
Notifications	<5	2.09 (55)	33.91 (90)	0.99 (46)	2.41 (10)	**0.49 (0.33–0.73)**	**0.07 (0.04–0.13)**
	5–19	2.24 (194)	18.37 (120)	1.33 (185)	1.46 (16)	**0.59 (0.48–0.73)**	**0.08 (0.05–0.13)**
	20–49	3.30 (604)	6.13 (48)	1.30 (404)	0.38 (5)	**0.39 (0.35–0.45)**	**0.06 (0.02–0.15)**
	50–64	1.63 (116)	2.36 (3)	0.66 (88)	0.81 (2)	**0.41 (0.31–0.54)**	0.29 (0.05–1.73)
	⩾65	1.01 (52)	0.00 (0)	0.35 (33)	0.98 (1)	**0.34 (0.22–0.52)**	–
	Total	2.44 (1021)	13.85 (261)	1.04 (756)	1.08 (34)	**0.43 (0.39–0.47)**	**0.07 (0.05–0.10)**
Hospitalisations	<5	0.19 (5)	16.99 (45)	0.26 (9)	0.62 (2)	1.45 (0.49–4.33)	**0.04 (0.01–0.16)**
	5–19	0.54 (47)	5.26 (35)	0.43 (44)	1.04 (8)	0.82 (0.54–1.23)	**0.18 (0.09–0.40)**
	20–49	1.95 (359)	4.51 (35)	0.89 (200)	1.72 (16)	**0.46 (0.39–0.55)**	**0.37 (0.20–0.66)**
	50–64	1.53 (108)	1.54 (2)	0.88 (87)	0.00 (0)	**0.61 (0.46–0.81)**	–
	⩾65	1.76 (91)	0.00 (0)	0.94 (65)	0.00 (0)	**0.55 (0.40–0.76)**	–
	Total	1.45 (610)	6.20 (117)	0.77 (405)	1.15 (26)	**0.54 (0.48–0.62)**	**0.18 (0.12–0.27)**
	Age group (years)	Pre-vaccination (2000–2005)		Post-vaccination[a]		Incidence rate ratio[b]	
		Non-Indigenous[c] (N)	Indigenous[c] (N)	Non-Indigenous[c] (N)	Indigenous[c] (N)	Non-Indigenous (95% CI)	Indigenous (95% CI)
(b) Non-targeted jurisdictions: New South Wales, Victoria, Tasmania and the Australian Capital Territory							
Notifications	<5	1.21 (55)	0.00 (0)	1.23 (92)	0.00 (0)	0.96 (0.69–1.33)	–
	5–19	2.21 (319)	1.96 (10)	1.79 (393)	0.57 (5)	**0.81 (0.70–0.94)**	**0.32 (0.11–0.95)**
	20–49	2.89 (907)	1.09 (6)	1.43 (720)	0.70 (7)	**0.50 (0.46–0.56)**	0.67 (0.23–1.99)
	50–64	1.12 (133)	0.00 (0)	0.77 (164)	0.86 (2)	**0.69 (0.55–0.87)**	–
	⩾65	1.07 (102)	2.07 (1)	0.64 (107)	0.00 (0)	**0.59 (0.45–0.78)**	–
	Total	2.12 (1516)	1.19 (17)	1.25 (1476)	0.55 (14)	**0.60 (0.56–0.64)**	**0.47 (0.23–0.95)**
Hospitalisations	<5	0.18 (8)	1.48 (3)	0.23 (12)	0.00 (0)	1.28 (0.52–3.14)	–
	5–19	0.53 (77)	0.81 (4)	0.61 (99)	0.28 (1)	1.18 (0.87–1.58)	0.20 (0.02–1.80)
	20–49	1.79 (562)	2.50 (14)	1.01 (383)	2.08 (15)	**0.60 (0.52–0.68)**	0.88 (0.42–1.82)
	50–64	1.56 (185)	0.90 (1)	1.15(177)	1.99 (4)	**0.76 (0.62–0.93)**	2.67 (0.30–23.88)
	⩾65	2.22 (211)	2.34 (1)	1.19 (142)	0.00 (0)	**0.54 (0.44–0.67)**	–
	Total	1.45 (1043)	1.61 (23)	0.94 (813)	1.10 (20)	**0.67 (0.61–0.73)**	0.70 (0.38–1.27)

N = number of cases.
Bold IRR denote significant reductions (p-value < 0.05).
[a] Post-vaccine period-Notifications: January 2006-December 2014; Hospitalisations: January 2006-June 2012.
[b] Comparison of pre- and post-vaccine periods.
[c] Average annual rate per 100,000 total population.

ing error. As recommended by the Australian Institute of Health and Welfare, all hospitalisation data was included for analyses of Indigenous status [30]. However, data relating to Indigenous status from the non-targeted jurisdictions should be interpreted with caution, as weighted completeness for Indigenous identification in public hospitals during 2011–12 was below the level considered acceptable (80%) in Tasmania, the Australian Capital Territory, and Victoria [30].

Declines in hepatitis A in Indigenous populations following targeted childhood immunisation programs have also been reported in the United States of America (USA), although without clear evidence of broader herd protection impacts on the non-Indigenous population [31–34]. However Indigenous Australians make up a greater proportion (2.4%) of the Australian population than Native Americans and Alaskan Natives do in the USA (0.9%) [33,35]. Substantial herd protection effects arising from universal childhood hepatitis A immunisation programs have been documented in Israel, Argentina and the USA, with the USA introducing a national universal program in 2006 following evidence of substantially higher decreases in incidence in states with universal programs already in place [36–40]. However, targeted hepatitis A vaccination programs have generally been estimated to be more cost-effective in lower incidence settings than universal programs [41]. The World Health Organization recommends mass vaccination programs in countries moving from high to intermediate hepatitis A endemicity, but targeted programs in countries with low endemicity [1]. The USA is the only low endemicity country of similarly high income to Australia that has introduced a universal childhood program, as of 2011 the hepatitis A notification rate in the USA was similar to that reported in Australia (0.4 and 0.6 per 100,000, respectively) despite reasonable vaccination coverage in the USA among children aged 19–35 months (78–87% one-dose coverage and 50–57% two dose coverage in 2011) [42]. In most Western European countries hepatitis A incidence has also declined to below 1.0 per 100,000, in the context of immunisation programs targeting only individuals at high risk [43]. Universal routine vaccination of children has been associated with increased age of infection, and hence risk of more severe disease [44,45]. In the context of the targeted Australian immunisation program we found no change in the median age of notified and hospitalised cases between pre- and post-vaccine periods.

The relatively low hepatitis A seroprevalence in the Australian population (approximately 55% in persons aged less than 70 years, from Victoria during 2008 [46]) leaves a large pool of susceptible individuals. Non-immune individuals in Australia, and other developed countries, remain at risk of hepatitis A, particularly when they travel to endemic countries and during foodborne outbreaks linked to the global food economy, such as those which occurred in Australia in 2009, associated with imported semi-dried tomatoes [9], in the USA in 2013, associated with imported pomegranate arils [37,47], and in Europe, Australia and New Zealand, associated with raw and frozen berries [7,48–51]. The majority of hepatitis A cases (ranging from 56% to 87% between 2010 and 2014) in Australia now acquire their infection while travelling to endemic countries. Increasing hepatitis A vaccine coverage among travellers will reduce the risk of importation and subsequent sec-

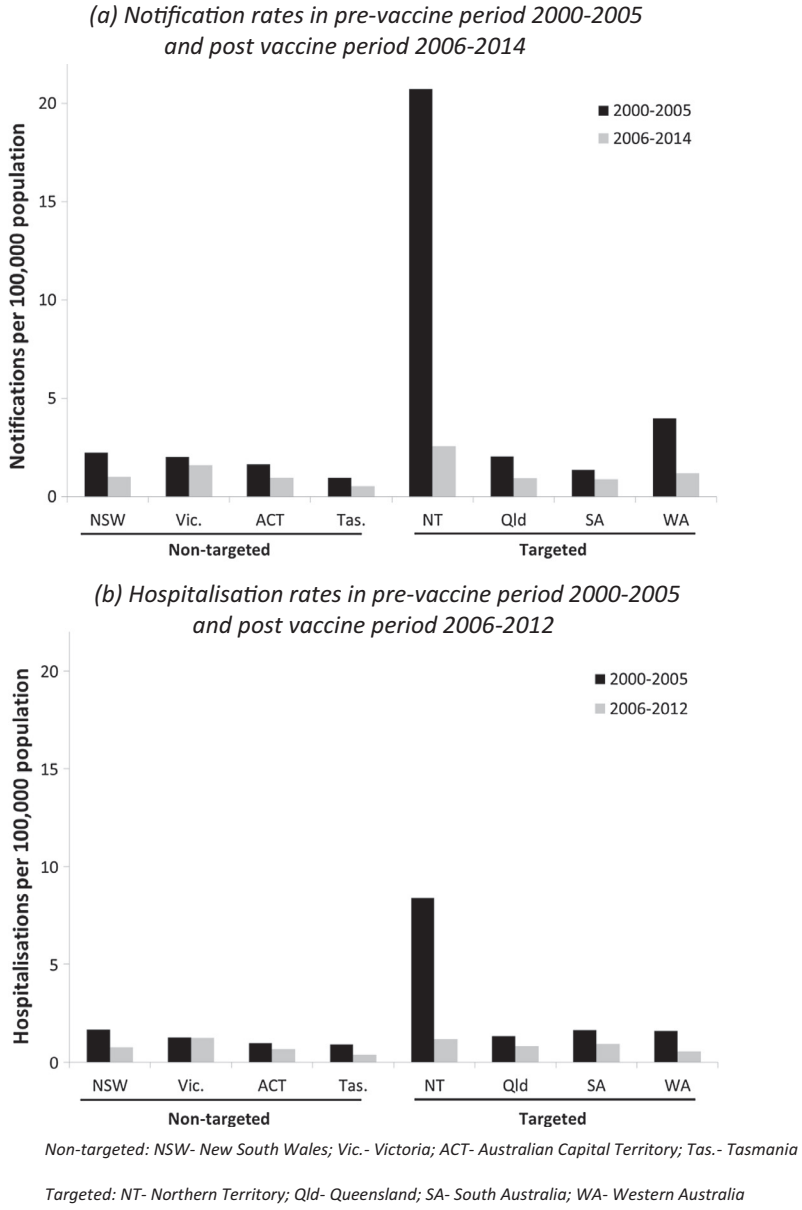

Fig. 2. Hepatitis A notification and hospitalisation rates by jurisdiction, and pre-/post-vaccine period, Australia, 2000–2014. (a) Notification rates in pre-vaccine period 2000–2005 and post vaccine period 2006–2014. (b) Hospitalisation rates in pre-vaccine period 2000–2005 and post vaccine period 2006–2012. Non-targeted: NSW - New South Wales; Vic. - Victoria; ACT - Australian Capital Territory; Tas. - Tasmania. Targeted: NT - Northern Territory; Qld - Queensland; SA - South Australia; WA - Western Australia.

ondary spread. However, this has proven difficult to achieve in Australia and further research is needed to inform effective strategies to increase community awareness of hepatitis A vaccines and access to vaccination services [28,29]. Foodborne outbreaks are also difficult to prevent, even with rigorous food safety standards in place, due to the difficulties involved in testing for hepatitis A virus in imported foodstuffs [52,53]. A universal infant hepatitis A immunisation program in Australia could help mitigate the impact of foodborne outbreaks, however, this would involve substantial cost and take decades to have its full effect.

5. Conclusions

In summary, the national hepatitis A immunisation program in Australia has had a significant impact in the targeted population, with evidence suggesting a broader herd protection effect. Ongoing surveillance is required to be sure that the current targeted immunisation strategy is maintaining satisfactory disease control.

Authors' contributions

CT, AD, EF and FB designed the study. CT reviewed the literature, conducted the statistical analyses, analysed the data and wrote the initial draft of the manuscript. AD, EF, BP and FB supervised the analysis and assisted with writing the manuscript. All authors contributed by making critical revisions to the manuscript and all have approved the final article.

Conflict of interest statement

The authors have no conflicts of interests to declare

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References

[1] World Health Organization. WHO position paper on hepatitis A vaccines–June 2012. Wkly Epidemiol Rec 2012;87(28–9):261–76.
[2] Heyman D. Control of communicable diseases manual. 20th ed. Washington, DC: American Public Health Association Press; 2015.
[3] Jacobsen KH, Koopman JS. Declining hepatitis A seroprevalence: a global review and analysis. Epidemiol Infect 2004;132(6):1005–22.
[4] Jacobsen KH, Wiersma ST. Hepatitis A virus seroprevalence by age and world region, 1990 and 2005. Vaccine 2010;28(41):6653–7.
[5] Amin J, Heath T, Morrell S. Hepatitis A in Australia in the 1990s: future directions in surveillance and control. Commun Dis Intell 1999;23:113–9.
[6] NNDSS Annual Report Working Group. Australia's notifiable disease status, 2014: annual report of the National Notifiable Diseases Surveillance System. Commun Dis Intell 2016;40(1):E48.
[7] Australian Government Department of Health. Hepatitis A and frozen berry products recall; 2015. Available from: <http://health.gov.au/internet/main/publishing.nsf/Content/ohp-hep-A-frozen-berry.htm> [accessed October 2015].
[8] Conaty S, Bird P, Bell G, Kraa E, Grohmann G, McAnulty J. Hepatitis A in New South Wales, Australia, from consumption of oysters: the first reported outbreak. Epidemiol Infect 2000;124(01):121–30.
[9] Donnan EJ, Fielding JE, Gregory JE, Lalor K, Rowe S, Goldsmith P, et al. A multistate outbreak of hepatitis A associated with semidried tomatoes in Australia, 2009. Clin Infect Dis 2012;54(6):775–81.
[10] Hanna JN, Humphreys JL, Hills SL, Richards AR, Brookes DL. Recognising and responding to outbreaks of hepatitis A associated with child day-care centres. Aust N Z J Public Health 2001;25(6):525–8.
[11] Lee D, Ashwell M, Ferson M, Beer I, McAnulty J. Hepatitis A outbreak associated with a Mothers' Day 'Yum Cha' meal, Sydney, 1997. NSW Public Health Bull 2004;15(1–2):6–9.
[12] Munnoch SA, Ashbolt RH, Coleman DJ, Walton N, Beers-Deeble MY, Taylor R. A multi-jurisdictional outbreak of hepatitis A related to a youth camp-implications for catering operations and mass gatherings. Commun Dis Intell 2004;28(4):521–7.
[13] Rowe SL, Tanner K, Gregory JE. Hepatitis A outbreak epidemiologically linked to a food handler in Melbourne, Victoria. Commun Dis Intell 2009;33(1):46–8.
[14] Stokes M-L, Ferson MJ, Young LC. Outbreak of hepatitis A among homosexual men in Sydney. Am J Public Health 1997;87(12):2039–41.
[15] Schultz R. Hepatitis A outbreak in Central Australia. NT Dis Control Bull 2005;12(4):4–7.
[16] The Australian Immunisation Handbook (updated June 2015). 10th ed. Canberra: Australian Government Department of Health; 2013.
[17] Hanna JN, Hills SL, Humphreys JL. Impact of hepatitis A vaccination of indigenous children on notifications of hepatitis A in north Queensland. Med J Aust 2004;181(9):482–5.
[18] Hanna JN, Warnock TH, Shepherd RW, Selvey LA. Fulminant hepatitis A in indigenous children in north Queensland. Med J Aust 2000;172(1):19–21.
[19] Royle J, Lambert SB. Fifty years of immunisation in Australia (1964–2014): the increasing opportunity to prevent diseases. J Paediatr Child Health 2015;51(1):16–20.
[20] Naidu L, Chiu C, Habig A, Lowbridge C, Jayasinghe S, Wang H, et al. Vaccine preventable diseases and vaccination coverage in Aboriginal and Torres Strait Islander people, Australia 2006–2010. Commun Dis Intell 2012;37:S1–95.
[21] Chiu C, Dey A, Wang H, Menzies R, Deeks S, Mahajan D, et al. Vaccine preventable diseases in Australia, 2005 to 2007. Commun Dis Intell 2010;34:S1–S167.
[22] Communicable Diseases Network Australia (CDNA); 2015. Available from: <http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-nndss-casedefs-cd_hepa.htm> [accessed October 2015].
[23] Australian Bureau of Statistics. Australian Demographic Statistics; 2014. Available from: <http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3101.0Sep%202014?OpenDocument> [accessed July 2015].
[24] Hull B, Dey A, Beard F, Menzies R, Brotherton J, Mcintyre P. Annual immunisation coverage report 2013. Sydney: NCIRS; 2015.
[25] Hull B, Deeks S, Menzies R, McIntyre P. Immunisation coverage annual report, 2007. Commun Dis Intell 2009;33(2):170–87.
[26] Smith P, Grabau J, Werzberger A, Gunn R, Rolka H, Kondracki S, et al. The role of young children in a community-wide outbreak of hepatitis A. Epidemiol Infect 1997;118(03):243–52.
[27] Biddle N, Markham F. Paper 9-Mobility; 2013. Available from: <http://caepr.anu.edu.au/sites/default/files/cck_indigenous_outcomes/2013/05/2011CensusPaper09_Mobility.pdf> [accessed November 2015].
[28] Ward K, McAnulty J. Hepatitis A: who in NSW is most at risk of infection? NSW Public Health Bull 2008;19(1–2):32–5.
[29] Zwar N, Streeton CL. Pretravel advice and hepatitis A immunization among Australian travelers. J Travel Med 2007;14(1):31–6.
[30] Australian Institute of Health and Welfare. Indigenous identification in hospital separations data: quality report Cat. no. IHW 90. Canberra: AIHW; 2013.
[31] Shouval D, Mikhaylov M, van Herck K. Hepatitis A vaccines - impact of universal childhood vaccination programmes. Eur Gastroenterol Hepatol Rev 2011;7(2):77–83.
[32] Modlin JF, Snider D, Clover RD, Centers for Disease Control Prevention. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). Morb Mortal Wkly Rep 1999;48:1–37.
[33] Bialek SR, Thoroughman DA, Hu D, Simard EP, Chattin J, Cheek J, et al. Hepatitis A incidence and hepatitis A vaccination among American Indians and Alaska Natives, 1990–2001. Am J Public Health 2004;94(6):996–1001.
[34] Raczniak GA, Bulkow LR, Bruce MG, Zanis CL, Baum RL, Snowball MM, et al. Long-term immunogenicity of hepatitis A virus vaccine in Alaska 17 years after initial childhood series. J Infect Dis 2013;207(3):493–6.
[35] MacIntyre CR, Burgess M, Isaacs D, McIntyre PB, Menzies R, Hull B. Epidemiology of severe hepatitis A in Indigenous Australian children. J Paediatr Child Health 2007;43(5):383–7.
[36] Dagan R, Leventhal A, Anis E, Slater P, Ashur Y, Shouval D. Incidence of hepatitis A in Israel following universal immunization of toddlers. JAMA 2005;294(2):202–10.
[37] Klevens RM, Denniston MM, Jiles-Chapman RB, Murphy TV. Decreasing immunity to hepatitis A virus infection among US adults: Findings from the National Health and Nutrition Examination Survey (NHANES), 1999–2012. Vaccine 2015;33(46):6192–8.
[38] Fiore AE, Wasley A, Bell BP. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recommen Rep 2006;55(7):1–23.
[39] Vacchino M. Incidence of Hepatitis A in Argentina after vaccination. J Viral Hepatitis 2008;15(Suppl. 2):47–50.
[40] Wasley A, Samandari T, Bell BP. Incidence of hepatitis A in the United States in the era of vaccination. JAMA 2005;294(2):194–201.
[41] Anonychuk AM, Tricco AC, Bauch CT, Pham B, Gilca V, Duval B, et al. Cost-effectiveness analyses of hepatitis A vaccine: a systematic review to explore the effect of methodological quality on the economic attractiveness of vaccination strategies. PharmacoEconomics 2008;26(1):17–32.
[42] Murphy T, Denniston M, Hill H, McDonald M, Klevens M, Elam-Evans L, et al. Progress toward eliminating hepatitis A disease in the United States. MMWR Suppl 2016;65(1):29.
[43] Gossner C, Severi E, Danielsson N, Hutin Y, Coulombier D. Changing hepatitis A epidemiology in the European Union: new challenges and opportunities. Euro Surveill 2015;20:1–6.
[44] Mellou K, Sideroglou T, Papaevangelou V, Katsiaflaka A, Bitsolas N, Verykouki E, et al. Considerations on the current universal vaccination policy against hepatitis A in Greece after recent outbreaks. PLoS ONE 2015;10(1):1–10.
[45] Martinelli D, Bitetto I, Tafuri S, Lopalco PL, Mininni RM, Prato R. Control of hepatitis A by universal vaccination of children and adolescents: an achieved goal or a deferred appointment? Vaccine 2010;28(41):6783–8.
[46] Heywood AE, Newall AT, Gao Z, Wood JG, Breschkin A, Nicholson S, et al. Changes in seroprevalence to hepatitis A in Victoria, Australia: a comparison of three time points. Vaccine 2012;30(42):6020–6.
[47] Collier MG, Khudyakov YE, Selvage D, Adams-Cameron M, Epson E, Cronquist A, et al. Outbreak of hepatitis A in the USA associated with frozen pomegranate arils imported from Turkey: an epidemiological case study. Lancet Infect Dis 2014;14(10):976–81.
[48] Calder L, Simmons G, Thornley C, Taylor P, Pritchard K, Greening G, et al. An outbreak of hepatitis A associated with consumption of raw blueberries. Epidemiol Infect 2003;131(01):745–51.
[49] Rizzo C, Alfonsi V, Bruni R, Busani L, Ciccaglione A, De Medici D, et al. Ongoing outbreak of hepatitis A in Italy: preliminary report as of 31 May 2013. Euro Surveill 2013;18(27):20518.
[50] Gillesberg LS, Soborg B, Midgley S, Steens A, Vold L, Stene-Johansen K, et al. Ongoing multi-strain food-borne hepatitis A outbreak with frozen berries as suspected vehicle: four Nordic countries affected, October 2012 to April 2013. Euro Surveill 2013;18(17):20467.
[51] Guzman-Herrador B, Jensvoll L, Einoder-Moreno M, Lange H, Myking S, Nygard K, et al. Ongoing hepatitis A outbreak in Europe 2013 to 2014: imported berry mix cake suspected to be the source of infection in Norway. Euro Surveill 2014;19(15):20775.
[52] Sánchez G, Bosch A, Pintó R. Hepatitis A virus detection in food: current and future prospects. Lett Appl Microbiol 2007;45(1):1–5.
[53] Bouwknegt M, Verhaelen K, Rzeżutka A, Kozyra I, Maunula L, von Bonsdorff C-H, et al. Quantitative farm-to-fork risk assessment model for norovirus and hepatitis A virus in European leafy green vegetable and berry fruit supply chains. Int J Food Microbiol 2015;198:50–8.